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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/738,378	12/17/2003	Francisco Javier Canada Vicinay	2798-1-001	7275

7590 01/10/2008  
KLAUBER & JACKSON  
4th Fl.  
411 Hackensack Avenue  
Hackensack, NJ 07601

EXAMINER
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UNDERDAHL, THANE E

ART UNIT	PAPER NUMBER
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1651

MAIL DATE	DELIVERY MODE
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01/10/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/738,378

Applicant(s)

VICINAY ET AL.

Examiner

Thane Underdahl

Art Unit

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 09 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-39 is/are pending in the application.
- 4a) Of the above claim(s) 33,35 and 38 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-32,34,36,37 and 39 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- 1) ☒ Certified copies of the priority documents have been received.
  - 2) ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/9/07 has been entered.

This Office Action is in response to the Applicant's request for continued examination received 10/09/07. Claims 1-39 are pending. Claims 33, 35 and 38 are withdrawn. No claims are cancelled. No claims have been amended. No claims are new.

### **Response to Applicant's Arguments— 35 U.S.C § 103**

In the response submitted by the Applicant, the 35 U.S.C § 103 (a) rejection of claims 1, 2, 3, 4, 21-24, 27-32, 34, 36, 37, and 39 over Reyes et al (U.S. Patent # 5, 994, 092) in view of Ponpipom et al. (U.S. Patent # 4, 228,274), and Crumpton et al. (Biochem J. 70(4) 1958, page 729) as supported by Chemindustry.com, the Applicant's arguments were considered but not found persuasive in light of additional support by Schippers et al. (Analytical Chem, 1981).

The Applicant argues and provides a sworn declaration under 37 C.F.R. 1.132 that it would not be in the purview of one of ordinary skill in the art to select or optimize the solvent system as claim. The Applicant states,

"The appropriate solvent depends on the type of molecules and the range of solvents that must be tested and can be very broad. The more customary solvents in sugars tend to be low molecular weight alcohols, water, ethyl acetate, hexane, and their mixtures."  
(Applicant's Response, page 2 last paragraph)

And continues to testify that this creates the problem that,

"a large number of solvents and mixtures thereof must be tested or screened before arriving at the appropriate solvent to use. In the case of the instant invention, acetone allows obtaining the product desired with a >99% degree of purity, which was not possible with more usual solvents." (Applicant's Response, page 3 top paragraph)

The Examiner has considered this line of argument as well as the submitted declarations and remains not persuaded. The Applicant did not address that the Examiner has found art in Crumpton et al. explicitly teach the use of aqueous acetone for recrystallization of low molecular weight sugars (Crumpton et al., page 732, col 2, paragraph 1). Furthermore while the Applicant does show >99% purity with their method this result is not unexpected in view of the teachings of Crumpton et al. who teach that their method of purifying their low molecular weight sugar with aqueous acetone provided a product that was optically pure under circular dichroism (**CD**) (Crumpton, page 732, col 2, 1<sup>st</sup> paragraph). While they do not provide a percentage to support their purity, one of ordinary skill in the art would recognize that optical purity achieved by this recrystallization method provides a substantially pure sugar, of which is close to that of the Applicant. Schippers et al. supports that optical purity and chemical purity are in close agreement (Schippers, Experimental section).

Therefore given the teachings of Crumpton et al. it was indeed in the purview of one of ordinary skill in the art to select acetone or aqueous acetone from other solvents to purify low molecular weight sugars. The motivation and rationale is provided by their successful purification of low molecular weight sugars. Furthermore since it is known in the art of Crumpton et al. that low molecular weight sugars can be purified by recrystallization in aqueous acetone it would have been obvious to someone skilled in the art to combine this known prior art element and achieved the predicted result of a purified sugar (KSR International Co. v. Teleflex Inc., 550 U.S.--, 82 USPQ2d 1385

(2007)). Therefore the rejection stands and is repeated below with modifications to address the Applicant's arguments.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 2, 3, 4, 21-24, 27-32, 34, 36, 37, 39 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Reyes et al (U.S. Patent # 5, 994, 092) in view of Ponpipom et al. (U.S. Patent # 4, 228,274), and Crumpton et al. (Biochem J. 70(4) 1958, page 729) as supported by Chemindustry.com ([www.chemindustry.com](http://www.chemindustry.com)) in light of additional support by Schippers et al. (Analytical Chem, 1981).

These claims are drawn to a method of production of 4-O- $\beta$ -D-galactopyranosyl-D-xylose and purification from an enzymatic reaction between  $\sigma$ -nitrophenyl-  $\beta$ -galactopyranoside and xylose with  $\beta$ -galactosidase acting as the catalyst.

The patent of Reyes et al. teach a method for the preparation of 4-O- $\beta$ -D-galactopyranosyl-D-xylose (4GPX) (See example 1, col 4). This method adds  $\sigma$ -nitrophenyl- $\beta$ -galactopyranoside to xylose in buffered water at pH=7 with  $\beta$ -galactosidase from *E. coli* into a reaction mixture. The reaction mix is incubated for 5 hours and 45 mins at 25 °C. After that time the reaction is heated to 100°C for 10 mins

and concentrated before being filtered on an activated carbon column with a water/ethanol gradient. This gradient isolates the 4-O-  $\beta$ -D-galactopyranosyl-D-xylose.

Claims 22-24 pertain to the amounts of D-xylose (claim 22),  $\beta$ -galactopyranoside (claim 23) and  $\beta$ -galactosidase (claim 24) added to the reaction solution. Reyes et al. already discusses the addition of these components in Example 1 in their patent (col 4 to col 5). Slight adjustments to the concentrations of the reaction mixture are rendered obvious in the absence of unexpected results or teachings of criticality since one of ordinary skill in the art would routinely optimize the reaction based on efficient use of enzyme and substrates to improve the cost to yield ratio.

Claims 27-31 pertain to the temperature conditions for the reaction of claim 1, which includes the following temperature ranges: constant temperature (claim 27), -5 °C to 40 °C (claim 28), lower than 0 °C (claim 29), -5 °C (claim 30), room temperature (claim 31). Reyes et al. teach in Example 1 of their patent (col 4 to col 5) that the reaction can be performed at constant room temperature (25 °C). One of ordinary skill in the art would recognize that the hydrolysis of the substrate,  $\sigma$ -nitrophenyl- $\beta$ -galactopyranoside by  $\beta$ -galactosidase will occur at any temperature in which the enzyme is active. This same artisan would also understand that the decrease of temperature will adjust the reaction rate. Therefore base on the time allotted for the reaction (i.e. performing the reaction overnight or over the lunch hour) one of ordinary skill in the art, through routine optimization would adjust the temperature accordingly.

Reyes et al. does not teach the crystallization of 4GPX. However crystallization is a common procedure for the purification of saccharides as taught by Ponpipom et al.

who crystallized glycopyranosides in either cold water or acetone (col 3, line 50).

Ponpipom et al. also teach that it is also possible to crystallize other glycopyranosides after a filtration step with diatomaceous silica (col 13, line 50) in solvents such as ethanol (col 10, line 68) or 2-propanone (col 13, line 44) or solvent mixtures such as ethyl acetate/ethyl ether (col 12, line 30). Diatomaceous silica is a synonym for Celite as supported by Chemindustry.com. Crumpton et al. teach that a disaccharide can be crystallized with aqueous acetone that is optically pure in CD spectroscopy (Crumpton, page 732, col 2, paragraph 1). Schippers et al. supports that optical purity and chemical purity are in close agreement (Schippers, Experimental section). With all these options available for the crystallization of saccharides, one of ordinary skill in the art would recognized that recrystallization is a common process for the isolation of saccharides and that the selection of solvent or mixture of solvents is a matter of routine optimization that depends on temperature, purity of the solvent and miscibility of the solvent systems used in the crystallization. Absent any teachings of criticality of the solvent selected and unexpected results one of ordinary skill in the art would have reasonable expectation of success in crystallizing disaccharides with the current available art. Please see M.P.E.P. § 2144.05 (II) and (KSR International Co. v. Teleflex Inc., 550 U.S.--, 82 USPQ2d 1385 (2007)) for further support.

Therefore the references listed above renders obvious claims 1, 2, 3, 4, 21-24, 27-32, 34, 36, 37, 39.

In response to the applicant's traversal of the 35 U.S.C § 103 rejection of claims 1, 5, 6, and 16-19 over Reyes et al (U.S. Patent # 5, 994, 092) in view of Ponpipom et al. (U.S. Patent # 4, 228,274), and Crumpton et al. (Biochem J. 70(4) 1958, page 729) as applied above and in further view of Wong-Madden et al. (U.S. Patent # 5,770,405) and Dahmen et al. (U.S. Patent # 4,675,392), the applicants arguments were considered but not found persuasive.

The Applicant argues that since the independent claim is found allowable because of the unexpected results in purity that, in turn, the dependent claims are allowable. However, as cited above this is not the case and the independent claims remain rejected.

The Applicant argues that Wong-Madden et al. teaches the use of their solvent mixture for silica gel and not active carbon. However, as stated in the action the solvent system of Wong-Madden et al. for the purification of oligosaccharides is very similar to the solvent system used by Reyes et al. that was used to purify sugars on an activated carbon column. The 37 C.F.R. 1.132 declaration discusses the economic and environmental impact of the solvents, but does not address whether either solvent systems will or will not adequately separate oligosaccharides on the activated carbon column. Since Reyes et al. does teach the use of a water/ethanol gradient to elute 4GPX from an activated carbon column and Wong-Madden et al. uses a similar solvent system of water/isopropanol/ethanol on silica gel. One of ordinary skill in the art would recognize from these references that the same solvent systems used for a silica gel column would work for an active carbon column since in the purification of



disaccharides. The rationale that the obviousness of this rejection holds is that one of ordinary skill in the art could combine these prior art elements and yield the predictable result (KSR International Co. v. Teleflex Inc., 550 U.S.--, 82 USPQ2d 1385 (2007)).

Therefore the rejection stands and is repeated below.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 5, 6, and 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Reyes et al (U.S. Patent # 5, 994, 092) in view of Ponpipom et al. (U.S. Patent # 4, 228,274), and Crumpton et al. ( Biochem J. 70(4) 1958, page 729) as applied above and in further view of Wong-Madden et al. (U.S. Patent # 5,770,405) and Dahmen et al. (U.S. Patent # 4,675,392).

These claims pertain to a method of isolation of 4GPX via a solid-liquid extraction using a column with an eluent and gradient of water/isopropanol.

Reyes et al., Ponpipom et al., and Crumpton et al. teach the enzyme assisted synthesis and purification via an activated carbon column and crystallization of 4GPX as detailed above.

Reyes et al. does teach the use of a water/ethanol gradient to elute 4GPX from an activated carbon column but not water/isopropanol as limited in claims 5 and 6.

However Wong-Madden et al. (U.S. Patent # 5, 770,405) shows that solvent mixes of water/isopropanol/ethanol are suitable for the separation of oligosaccharides (col 12, table 2). It would be obvious to one skilled in the art to replace ethanol in the method of Reyes et al. with isopropanol since Wong-Madden et al. shows that these act as art defined equivalents for the separation of saccharides.

Claims 16-19 discuss the purification of 4GPX on an activated carbon column which is taught by Reyes et al. (Example 1, col 5, line 3) who uses a solvent gradient of water/ethanol to elute 4GPX. As mentioned above Wong-Madden et al. shows that it is obvious to replace the water/ethanol gradient with an isopropanol/water solvent mixture. However neither directly teaches the specifics of the solvent gradient in claims 17 nor the amount of activated carbon to use in claim 18. These items are result effective variables optimized by routine experimentation by one or ordinary skilled in the art. The average skilled artisan would recognize that the solvent gradient will depend on the size of the column particles, the length and width of the column as well as the time allotted for the separation. The amount of activated carbon to use will depend on the perceived yield of 4GPX and the loading amounts of reaction mixture the column can bear to separate. Therefore the references listed above renders obvious claims 1, 5, 6, and 16-19.

In response to the Applicant's traversal of the 35 U.S.C § 103 rejection of amended claims 1, 7-15 over Reyes et al (U.S. Patent # 5, 994, 092) in view of Ponpipom et al. (U.S. Patent # 4, 228,274), Crumpton et al. ( Biochem J. 70(4) 1958,

page 729) Wong-Madden et al. (U.S. Patent # 5,770,405) and Dahmen et al. (U.S. Patent # 4,675,392) as applied above and in further view of Rao et al. (Qual. Plant. - Pl.Fds.hum.Nutr. XXVIII 4:293-303, 1979) the Applicant's arguments were considered but not found persuasive.

The Applicant argues that since the independent claim is found allowable because of the unexpected results in purity that, in turn, the dependent claims are allowable. However, as cited above this is not the case and the independent claims remain rejected.

The Applicant argues that one of ordinary skill in the art would not consider using activated carbon to purify low molecular weight sugars in view of the pervading art that supports the use of silica gel. However the art cited by the Examiner shows that using silica gel, activated carbon or soxhlet extractors are used to purify sugars and are elements known in the art to yield the predictable result. Therefore it would remain obvious to use either or a mixture of the elements to isolate sugars since this is simple either a substitution or a combination of prior art elements that will yield the predictable result of a purified sugar (KSR International Co. v. Teleflex Inc., 550 U.S.--, 82 USPQ2d 1385 (2007)). Therefore the rejection stands and is repeated below.

Therefore the following rejection is upheld and is repeated here. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the

subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 7-15 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Reyes et al (U.S. Patent # 5, 994, 092) in view of Ponpipom et al. (U.S. Patent # 4, 228,274), Crumpton et al. (Biochem J. 70(4) 1958, page 729) Wong-Madden et al. (U.S. Patent # 5,770,405) and Dahmen et al. (U.S. Patent # 4,675,392) as applied above and in further view of Rao et al. (Qual. Plant.-Pl.Fds.hum.Nutr. XXVIII 4:293-303, 1979).

These claims pertain to the method of extracting the 4GPX with celite and a Soxhlet extractor.

Claim 7 depends from claim 1 and limits the additional purification of the disaccharide to include the addition of celite and to the reaction mixture and extraction of the disaccharide with a Soxhlet extractor. Neither of these are taught by Reyes et al. However, the use of Soxhlet extractors and celite are known in the art as methods to purify saccharides as taught by Rao et al. (page 294, 3<sup>rd</sup> paragraph and 295 1<sup>st</sup> paragraph respectively) as well as previously mentions by Ponpipom et al. above. Rao et al. also uses a non-polar/polar solvent mix of chloroform and methanol. However one of ordinary skill in the art would recognize that the main requirement for a solvent for Soxhlet extraction is that the compound be soluble in the hot solvent. It would be obvious to one skilled in the art to select other solvents or solvent mixes, known to dissolve saccharides such as those listed above by Ponpipom et al., or by those listed

by Dahmen et al. who lists multiple solvents that other disaccharides are soluble in such as ethyl acetate (col 13, line 67) or solvent systems such as isooctane/ethyl acetate (col 14, line 42) for use in Soxhlet extraction. Again it would be a matter of routine optimization by the artisan to select solvents known in the art that dissolved saccharides (see M.P.E.P. § 2144.05 (II)) for Soxhlet extraction and absent any evidence to the criticality of solvent selection for the extraction or teaching of an unexpected result, one of ordinary skill in the art would have a reasonable expectation of success.

The amount of solvent used to elute the disaccharide from celite is also a matter of routine optimization by one of skill in the art. The volume of solvent to remove the disaccharide would depend on the size of the celite particles, the purity of the solvent and the temperature of the solvent and the amount of disaccharide absorbed on the celite.

Also a matter of routine optimization is the amount of celite to use in the extraction of the disaccharide. One of ordinary skill in the art would recognize that overloading the column would not accomplish the goal of purifying the disaccharide. Therefore this artisan would know the loading parameters of the celite or carbon-celite used in the experiment. He/she would also recognize that the loading amount of celite necessary for the purification would depend on the size and surface area of the celite particles. The skilled artisan would recognize that he/she must use the necessary amount of celite to purify the disaccharide base on the prospective yield. Larger reaction batches would require larger amounts of celite.

Claims 11 and 15 limit that the carbon in the activated carbon-celite column must be deactivated with HCl. One of ordinary skill in the art would recognize that the procedure for deactivating the column is a matter of routine optimization that would depend on the amount of the activated carbon in the column and the size of the column and recommendations from the manufacture. It would also be dependant on the size and surface area of the carbon particles since this would determine how many theoretical plates were available for the adsorption and separation of the disaccharide.

In response to the applicant's traversal of the 35 U.S.C § 103 rejection of amended claims 25 and 26 over Reyes et al (U.S. Patent # 5, 994, 092) in view of Ponpipom et al. (U.S. Patent # 4, 228,274), Crumpton et al. ( Biochem J. 70(4) 1958, page 729), Dahmen et al. (U.S. Patent # 4,675,392), Rao et al. (Qual. Plant-Pl.Fds.hum. Nutr. XXVIII, 4: 1979, page 293) and Wong-Madden et al. (U.S. Patent # 5,770,405) in further view of Gabelsberger et al (FEMS Letters, 109(2-3), page 131, 1993), Fujimoto et al. (Glycogonjugate Journal 15, page 155, 1998) and Yoshitake et al.(Eur. J. Biochem. 101, page 395, 1979) the Applicant's arguments were considered but not found persuasive.

The Applicant refers to the previous arguments made in their response that have been addressed above and provides no further argument. However, the previous arguments were found not persuasive and in the absence of new arguments here, remain not persuasive for claims 25 and 26. Therefore the rejection stands and is repeated below.

Therefore the following rejection is upheld and is repeated here. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 25 and 26 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Reyes et al (U.S. Patent # 5, 994, 092) in view of Ponpipom et al. (U.S. Patent # 4, 228,274), Crumpton et al. ( Biochem J. 70(4) 1958, page 729), Dahmen et al. (U.S. Patent # 4,675,392), Rao et al. (Qual. Plant-Pl.Fds.hum. Nutr. XXVIII, 4: 1979, page 293) and Wong-Madden et al. (U.S. Patent # 5,770,405) in further view of Gabelsberger et al (FEMS Letters, 109(2-3), page 131, 1993), Fujimoto et al. (Glycogonjugate Journal 15, page 155, 1998) and Yoshitake et al.(Eur. J. Biochem. 101, page 395, 1979).

These claims are drawn to the addition of cosolvents DMF, DMSO and dioxane to the reaction medium in the method of claim 1.

Reyes et al. and references listed above teach the method of claim 1 from which 25 and 26 depend. Reyes et al. teach the use of a phosphate buffer as the reaction solution but not with a cosolvent. However three other references that involve reactions using  $\beta$ -galactosidase use DMF (Fujimoto et al., page 157, col 1, 1<sup>st</sup> and 3<sup>rd</sup> paragraphs), DMSO (Gabelsberger et al. page 133, col 1, 1<sup>st</sup> paragraph) and dioxane

(Yoshitake et al., page 396, col 2 line 1) in the formulation of their phosphate buffer. All three of these reactions use the organic solvent/phosphate buffer system successfully with  $\beta$ -galactosidase to hydrolyze a substrate. It would have been obvious to someone skilled in the art to use either of the three solvents in the phosphate buffer in the method of Reyes et al. Since all three share the same goal of hydrolyzing a substrate with  $\beta$ -galactosidase. Each provides a reasonable expectation of success since each accomplishes the hydrolysis of their substrate using their phosphate buffer cosolvent.

The amount of the cosolvent ranges from 20% in Fujimoto et al. to 2% in Yoshitake et al. One of ordinary skill in the art would recognize that the amount of DMSO is an optimizable parameter and that the amount of solvent in the phosphate buffer would depend on the amount of enzymes in the solution along with the solubility tolerance of the substrate in the buffer as the co-solvent increases or decreases. Therefore claim 26 is rendered obvious since one of ordinary skill in the art would meet the limitation through routine optimization of the co-solvent in the reaction mixture.

Therefore the references listed above renders obvious claims 25 and 26.

In summary no claims, as written, are allowed for this application.

**In response to this office action the applicant should specifically point out the support for any amendments made to the disclosure**, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.



Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

#### CONTACT INFORMATION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thane Underdahl whose telephone number is (571) 272-9042. The examiner can normally be reached Monday through Thursday, 8:00 to 17:00 EST.

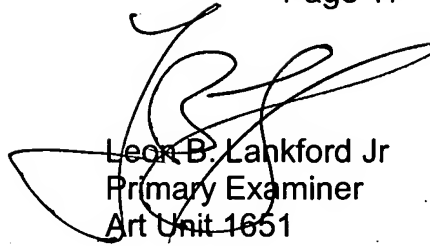
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Thane Underdahl  
Art Unit 1651



Leon B. Lankford Jr  
Primary Examiner  
Art Unit 1651